REMARKS

Claim Amendments

Claims 1, 4-25, 31, and 32 are pending in this application. Claims 2-3 and 26-30 were previously cancelled without prejudice or disclaimer. Claims 8 and 31-32 are cancelled herein with this response without prejudice or disclaimer. New claims 33-42 have been added. With this response, claims 1, 4-7, 9-25, and 33-42 are currently pending.

Claims 1, 4-7, 9, 10, 14, 17, and 18 have been amended herein. Claim 1 has been amended to recite that the assay system comprises mammalian cultured cells or a non-human animal wherein the assay system includes an assay that detects an agent-biased change in branching morphogenesis and to recite that the MBM gene is MAPK4. Support for the amendments are found throughout the application and in the original claims.

Claim 4 has been amended to recite that the MBM gene is MAPK4, that the assay system includes a binding assay comprising a MAPK4 polypeptide, and that the candidate test agent is an anti-MAPK4 antibody. Support for the amendments are found throughout the application and in the original claims.

Claim 5 has been amended to recite that the MBM gene is MAPK4. Claim 6 has been amended to recite that the assay system includes an expression assay comprising a MAPK4 nucleic acid and that the candidate test agent is an antisense oligomer against MAPK4. Support for these amendments are found throughout the application and in the original claims.

Claim 7 has been amended to provide proper antecedent basis. Claims 9, 10, and 14 have been amended to correct their dependencies. Claim 18 has been amended to correct a grammatical error.

Claim 17 has been amended to specify that the cultured cells of the second assay system are mammalian cells.

New claim 33 recites the method of claim 1 except that the MBM polypeptide or nucleic acid is selected from the group consisting of CaMKIIg, CNK, F1122055, FZD7, GSK3B, HIPK3, KIT, MAPK1, MAPK10, L0C160848, MAPK6, NEK4, NTRK2, PDK4, PKMYT1, PRKACB, PRKACA, PRKCA, PRKCD, PTK9L, PTK9, RAF1, STK24,

STK25, STK38L, STK38, L0C220231, TLK2, CDC7L1, and PRKACG. Support for claim 33 can be found throughout the specification.

New claim 34 recites the method of claim 4 except that the MBM polypeptide or nucleic acid is selected from the group consisting of CaMKIIg, CNK, F1122055, FZD7, GSK3B, HIPK3, KIT, MAPK1, MAPK10, L0C160848, MAPK6, NEK4, NTRK2, PDK4, PKMYT1, PRKACB, PRKACA, PRKCA, PRKCD, PTK9L, PTK9, RAF1, STK24, STK25, STK38L, STK38, L0C220231, TLK2, CDC7L1, and PRKACG, the assay system includes a binding assay comprising an MBM polypeptide, and the candidate test agent is an antibody. Support for claim 34 can be found throughout the specification.

New claim 35 recites the method of claim 6 except that the MBM polypeptide or nucleic acid is selected from the group consisting of CaMKIIg, CNK, F1122055, FZD7, GSK3B, HIPK3, KIT, MAPK1, MAPK10, L0C160848, MAPK6, NEK4, NTRK2, PDK4, PKMYT1, PRKACB, PRKACA, PRKCA, PRKCD, PTK9L, PTK9, RAF1, STK24, STK25, STK38L, STK38, L0C220231, TLK2, CDC7L1, and PRKACG, the assay system includes an expression assay comprising a MBM nucleic acid, and the candidate test agent is an antisense oligomer. Support for claim 35 can be found throughout the specification.

New claim 36 recites a method of identifying a candidate branching morphogenesis modulating agent comprising (a) providing a first assay system comprising cultured mammalian cells expressing a MAPK4 polypeptide or nucleic acid; (b) contacting the cultured mammalian cells with a test agent; (c) measuring the activity of the MAPK4 polypeptide or the expression of the MAPK nucleic acid in the cultured mammalian cells, wherein a difference between the activity or expression of the MAPK4 polypeptide or nucleic acid in the presence of the test agent compared to its absence identifies the test agent as a candidate branching morphogenesis modulating agent; (d) providing a second assay system comprising cultured mammalian cells or a non-human animal expressing a MAPK4 polypeptide or nucleic acid capable of detecting a change in activity associated with branching morphogenesis; (e) contacting the second assay system with the test agent of (b) or an agent derived therefrom; and (f) measuring the activity associated with branching morphogenesis in the cultured cells or the non-human animal, wherein a difference between the activity associated with branching morphogenesis in the presence of

the test agent or agent derived therefrom compared to its absence confirms the test agent as a candidate branching morphogenesis modulating agent. Support for claim 36 can be found throughout the specification and in original claim 17.

New claim 37 recites the method of claim 36, wherein the second assay system detects an activity selected from the group consisting of cell proliferation, cell cycling, apoptosis, tubulogenesis, cell migration, cell sprouting and response to hypoxic conditions. Support for claim 37 can be found throughout the specification and in original claims 17 and 20.

New claim 38 recites the method of claim 37, wherein the second assay system detects tubulogenesis or cell migration or cell sprouting, and comprises the step of testing the cellular response to stimulation with at least two different pro-angiogenic agents. Support for claim 38 can be found throughout the specification and in original claims 17 and 21.

New claim 39 recites the method of claim 37, wherein the second assay system detects tubulogenesis or cell migration, and wherein cells are stimulated with an inflammatory angiogenic agent. Support for claim 39 can be found throughout the specification and in original claims 17 and 22.

New claim 40 recites the method of claim 36, wherein the second assay system comprises a non-human animal. Support for claim 40 can be found throughout the specification and in original claims 17 and 23.

New claim 41 recites the method of claim 40, wherein the second assay system includes a matrix implant assay, a xenograft assay, a hollow fiber assay, or a transgenic tumor assay. Support for claim 41 can be found throughout the specification and in original claims 17 and 24.

New claim 42 recites the method of claim 41, wherein the second assay system includes a transgenic tumor assay that includes a mouse comprising a RIP 1-Tag2 transgene. Support for claim 42 can be found throughout the specification and in original claims 17 and 25.

The claim amendments are made solely in an effort to advance prosecution and are made without prejudice or disclaimer, without intent to acquiesce in any rejection of record, and without intent to abandon any previously claimed subject matter. Additionally, these amendments and cancellation are not and should not be construed as admissions regarding the patentability of the claimed or canceled subject matter. Applicants reserve the right to pursue the subject matter of previously presented claims in this or in any other appropriate patent application. No new matter has been added by way of these amendments. Accordingly, Applicants respectfully request the entry of the amendments presented.

Claim Objections

Claims 1, 4-25, 31 and 32 were objected to for reciting non-elected species beyond that MAPK4. Claims 31 and 32 have been cancelled rendering the objection moot as to these claims. Claims 1, and 4-25, as amended, are drawn to assays comprising a MAPK4 polypeptide or nucleic acid. Applicants respectfully request withdrawal of the claim objections.

The 35 USC § 102(b) Rejections

Peng et al.

Claim 1 remains rejected under 35 USC § 102(b), as allegedly being anticipated by Peng et al. (J. Neurochem, 1996, 66: 1191-1197). Applicants respectfully traverse the rejection.

Under 35 U.S.C. § 102, a claim is anticipated only if each and every element as set forth in the claim is found in a single art reference. *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 631, 2 USPQ2d 1051, 10533 (Fed. Cir. 1987); *In re Recombinant DNA Technology Patent and Contract Litigation*, 30 USPQ2d 1881 (S.D. Ind.1993) ("A patent is anticipated only if all the elements and limitations of the claims are found within a single, prior art reference. No difference may exist between the claimed invention and the

reference disclosure, as viewed by a person of ordinary skill in the field of invention."); *Structural Rubber Products Co. v. Park Rubber Co.*, 749 F.2d 707, 716 (Fed. Cir. 1984) (All elements of the claimed invention must be contained in a single prior art disclosure and must be arranged in the prior art disclosure as in the claimed invention); M.P.E.P § 2131. The identical invention must be described or shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); *Chester v. Miller*, 15 USPQ2d 1333 (Fed. Cir. 1990); M.P.E.P. § 2131.

The method of claim 1 requires, among other things, the use of an assay that detects an agent-biased change in branching morphogenesis. Peng et al. teaches that certain growth factors promote tyrosine phosphorylation of ERK4 (MAPK4), however, it fails to recognize a connection between MAPK4 and branching morphogenesis and fails to employ an assay that detects an agent-biased change in branching morphogenesis.

Peng et al does not teach each and every element of claim 1 and thus does not anticipate the claimed invention. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejections based on Peng et al.

Petersen et al.

Claims 1 and 5 remain rejected under 35 USC § 102(b), as allegedly being anticipated by Petersen et al. (Cell, 2000, 103: 1111-1120). Applicants respectfully traverse the rejections.

The methods of claims 1 and 5 employ the use of an assay system comprising mammalian cultured cells or a non-human animal expressing a MBM polypeptide or nucleic acid, which system includes an assay that detects an agent-biased change in branching morphogenesis. The teaching in Petersen is limited to the expression of MAPK4 in plant cells. Further, Petersen fails to recognize a connection between MAPK4 and branching morphogenesis and fails to employ an assay that detects an agent-biased change in branching morphogenesis.

Petersen et al does not teach each and every element of claim 1 or claim 5 and thus does not anticipate the claimed invention. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejections based on Petersen et al.

Takeishi et al.

Claim 1 remains rejected under 35 USC § 102(b), as allegedly being anticipated by Takeishi et al. (J. Mol Cell Biol, 2001, 33: 1637-1648) as evidenced by Gonzales et al. (FEBS Lett, 1992, 304: 170-178). Applicants respectfully traverse the rejection.

The method of claim 1 employs the use of an assay system comprising mammalian cultured cells or a non-human animal expressing a MBM polypeptide or nucleic acid, which system includes an assay that detects an agent-biased change in branching morphogenesis. Takeishi et al. fails to recognize a connection between MAPK4 and branching morphogenesis and fails to employ an assay that detects an agent-biased change in branching morphogenesis. Likewise, Gonzales fails to teach the claimed invention, including failing to recognize a connection between MAPK4 and branching morphogenesis.

Takeishi et al does not teach each and every element of claim 1 and thus does not anticipate the claimed invention. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejections based on Takeishi et al as evidenced by Gonzales et al.

Lee et al.

Claim 1 remains rejected under 35 USC § 102(b), as allegedly being anticipated by Lee et al. (Mol Cell Biol, 1999, 19: 1973-1980) as evidenced by Gonzales et al. (FEBS Lett, 1992, 304: 170-178). Applicants respectfully traverse the rejection.

The method of claim 1 employs the use of an assay system comprising mammalian cultured cells or a non-human animal expressing a MBM polypeptide or nucleic acid, which system includes an assay that detects an agent-biased change in branching morphogenesis. Lee et al. fails to recognize a connection between MAPK4 and branching

morphogenesis and fails to employ an assay that detects an agent-biased change in branching morphogenesis. Gonzales et al. also fails to recognize a connection between MAPK4 and branching morphogenesis and thus fails to teach the claimed invention.

Lee et al does not teach each and every element of claim 1 and thus does not anticipate the claimed invention. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejections based on Lee et al as evidenced by Gonzales et al.

Whelan et al.

Claims 31 and 32 remain rejected under 35 USC § 102(b), as allegedly being anticipated by Whelan et al. (Mol Biol Cell, 2000, 11 supp: 465a). Without acceding to the merits of the rejection, claims 31 and 32 have been cancelled, rendering the rejections moot. Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 102(b) rejections based on Whelan et al.

CONCLUSION

In view of the above remarks, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

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